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In vivo profile of the human leukocyte microRNA response to endotoxemia

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Background

To gain insight into microRNAs (miRNAs) involved in the regulation of the human innate immune response, we have screened for differentially expressed miRNAs in circulating leukocytes in an *in vivo* model of acute inflammation triggered by *E. coli* lipopolysaccharide (LPS) infusion.

Material and methods

Leukocyte RNA was isolated from venous blood samples obtained from healthy male volunteers before and 4 hours after LPS-infusion. After fluorescence labeling, RNA samples were hybridized to microarrays containing capture probes for measuring the abundance of more than 600 human miRNAs. Target genes were predicted for differentially expressed miRNAs and then compared to changes in genome-wide expression levels, which had been established in a previous study.

Results

Data analysis revealed that five miRNAs consistently responded to LPS-infusion, four of which were down-regulated (miR-146 b, miR-150, miR-342, and let-7 g) and one was up-regulated (miR-143). By correlating to measured LPS-induced changes of the leukocyte transcriptome, we next searched for predicted target genes, whose stability might be under (co-)control by these miRNAs. We found that the rapid transcriptional activation during acute inflammation of select genes, such as the gene encoding interleukin-1 receptor-associated kinase 2 (IRAK2) might be facilitated by decreased levels of LPS-responsive miRNAs. The increased level of miR-143 might be associated with the pronounced down-regulation of the B-cell CLL/lymphoma 2 (BCL2) gene expression during LPS endotoxemia, and could further be involved in the translational silencing of several other predicted inflammation-related target genes.

Conclusion

This is the first *in vivo* study to demonstrate relative abundance of miRNA levels in peripheral blood leukocytes during acute LPS-induced inflammation. The miRNAs and their potential target genes identified herein contribute to the understanding of the complex transcriptional program of innate immunity initiated by pathogens.